PB81-112690

Endrin: Position Document 1

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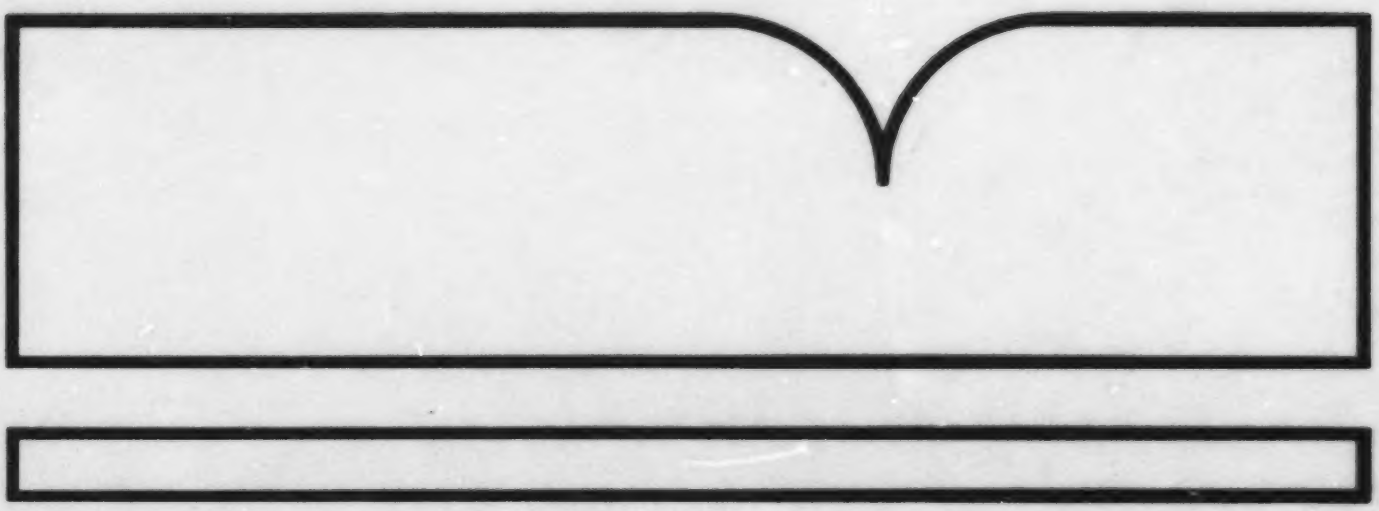

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Preliminary Risk Assessment: Examination of possible unreasonable risks associated with uses of pesticide and a gathering of all available information to determine whether or not this or any other risk does exist. Initiates literature search and evaluates risk data. Limited information on exposure to forecast extent of risk.

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Position Document #1 on Endrin

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I. BACKGROUND

A. Chemical/Physical Properties

Endrin (Hexachloroepoxy-octahydro-endo,endo-dimethanonaphthalene) belongs to the cyclodiene class of chlorinated chemical pesticides. Endrin is a stereoisomer of dieldrin. Much like its chemical relatives, it is a nonpolar compound, slightly soluble in water (230 ug/l at 25°C), highly soluble in lipids and strongly adsorbed on organic particulate matter such as soil particles.

B. Environmental Characteristics

Endrin appears to be somewhat less persistent in soil than dieldrin (Appendix A). Like dieldrin, endrin is readily concentrated from water by fish. Although extensive data are not available, endrin appears to be eliminated more rapidly than dieldrin from both fish and mammals. (Appendix B). It has been recently postulated that a metabolite of endrin in mammals, 12-ketoendrin, may be the main cause of acute toxicity (Appendix C). Little data exist on 12-ketoendrin and other metabolites since analytical detection methods have not been routinely used in monitoring studies. While adequate methodologies exist for environmental monitoring of endrin, there has been little actual monitoring in wildlife. Currently, there appears to be little evidence of human adipose tissue storage of endrin.

C. Registered Uses

Currently there are a total of 115 EPA-registered products, containing endrin as the active ingredient (see Appendix N). They are primarily used for the control of insects on cotton, small grain crops, sugarcane and ornamentals. In addition, endrin is registered for use as a ground spray to control orchard mice, as a perch treatment to control birds around buildings, and as a conifer seed treatment to repel mice. There are thirty-six applications for federal registration of state-registered products. The state products are registered for a variety of uses.

Based on reported production in 1974, about 720,000 lb active ingredient were used on cotton, 240,000 lb on small grain, and 40,000 lb on orchards. Other uses presumably involved much smaller quantities. Production figures for state-registered products are not available.

D. Production

Information concerning production, sales and distribution which is required to be submitted to EPA by §7(c) of the FIFRA is entitled to confidential treatment under the provision of §7(d) and §10 of the FIFRA. Accordingly such information may not be made available to the public. The production information concerning

endrin has been summarized in a separate memorandum for internal use by EPA (Appendix D).

In 1974, only 25 of the 61 EPA-registered producers reported production under 40 of the 115 registrations. Several producers including Shell Chemical Company have represented to EPA that they planned no production for 1975. These data suggest that use of endrin may have reached a peak in 1973.

II. REGULATORY HISTORY

Historically, serious concern over the environmental impacts from endrin can be traced to massive fish kills in the lower Mississippi in the early 1960's. In 1969 the Report of the Secretary of Health, Education, and Welfare's Commission on Pesticides and Their Relationship to Environmental Health (Mrak Commission, December 1969) listed endrin among several pesticides which "are persistent and cause or can cause contamination of the environment and damage to various life forms within it." The Commission recommended that the usage of these persistent pesticides be restricted "to specific essential uses which create no known hazard to human health or to the quality of the environment." (Recommendation 4, p. 9.)

Endrin's potential hazards to wildlife have been recognized and under active review by the EPA since 1971. No regulatory action has been taken by EPA.

Public comment on the risks and benefits of endrin use was solicited in a March 18, 1971, Federal Register Notice. An internal review of endrin was completed by the Criteria and Evaluation Division (CED) in 1973 (Appendix JJ). On November 8, 1973, the Director of CED recommended that the Agency seek to have formulations of endrin kept separate from those of methyl parathion and cancel all uses other than those for conifer seed treatment, control of pale western cutworms on small grain, avicidal treatment of bird perches, and control of orchard mice (Appendix E). No regulatory action was taken.

On July 31, 1975, the Environmental Defense Fund (EDF) and the National Audubon Society (NAS) petitioned the Agency to suspend or cancel all uses of endrin (Appendix F). Velsicol Chemical Corporation responded to this petition on November 10, 1975 (Appendix G). On April 30, 1976, the EDF renewed its petition. (Appendix H).

Pursuant to Section 307(a) of FWPCA, the Agency has proposed water effluent standards for endrin. The proposed ambient water quality criterion value is 0.004 ug/l (41 FR 23576, 23594, June 10, 1976.)

An update of the ecological hazards of endrin was initiated in 1975. Reports were received that fatality to brown pelicans in Louisiana was linked to endrin usage (Appendix I). The project manager has consulted with staff

from EPA Region VI, the Louisiana State University (LSU) and the Louisiana State Wildlife and Fisheries Commission concerning fatalities of brown pelicans that occurred in the spring of 1975 (Appendix J). In addition, discussions have been held with the Director and staff of the Patuxent Wildlife Research Center regarding the pelican deaths and copies of autopsy and residue analyses have been received (Appendix K).

The U.S. Fish and Wildlife Service has also supplied reports of recent tests conducted in collaboration with the U.S. Forest Service to evaluate the hazards of endrin-treated conifer seeds to birds (Appendix L). Staff members at the North Carolina State University have been consulted on the status of substitute chemicals and management practices to reduce pine mouse damage in orchards (Appendix M).

A working group with representatives from all relevant divisions and offices of EPA was formed to prepare this position document. Dr. Albert, Chairman of the Cancer Assessment Group, was asked to evaluate the data on oncogenicity, and the Validation Committee of CED was asked to review both chronic and acute data. As set forth in this position document and the accompanying notice of rebuttable presumption, the working group concurs in each of Dr. Albert's conclusions; it concurs in part and non-concurs in part with the Validation Committee's conclusions (Appendix X, Y).

III. SUMMARY OF SCIENTIFIC EVIDENCE OF REBUTTABLE PRESUMPTION CRITERIA

A. Chronic Toxicity

(1) Oncogenic Effects in Test Animals.

40 CFR Section 162.11(a)(3)(ii)(A) provides: "A rebuttable presumption shall arise if a pesticide's ingredient(s) . . . [i]nduces oncogenic effects in experimental mammalian species or in man as a result of oral, inhalation or dermal exposure . . . ."[1/]

EPA is aware of two oncogenicity studies with endrin which indicate that endrin induces oncogenic effects in both mice and rats as a result of oral exposure. The studies are an unpublished Food and Drug Administration (FDA) rat study with subsequent reanalysis performed for EPA (Appendixes O and P) and a Kettering mouse study (Appendix Q). In addition, five other studies contain some comment regarding oncogenicity, but are either inconclusive or, in light of the above data, insufficient to show endrin to be not oncogenic.

The CED Validation Committee reviewed the Kettering study and the study by Deichmann (Appendix R) and recommended that an oncogenic presumption should be issued (Appendix X); however, several months later the Committee reversed its

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1/ The term oncogenic is defined in 40 CFR Section 162.3(bb) as "the property of a substance or a mixture of substances to produce or induce benign or malignant tumor formulations in living animals."

recommendation (Appendix Y). This reversal was based upon an incorrect interpretation of the regulations (Appendix Z). Dr. Albert reviewed the Kettering study, Dr. Reuber's histopathological analysis of the FDA study, and the results of the EPA statistical analyses of each.

(a) Kettering Mouse Study

In a 1970 study performed by Kettering Laboratory using 1600 mice, both sexes of two strains of mice were fed diets containing 3.0 and 0.3 ppm endrin, and an equal number were used as controls. The report concluded that endrin did not accelerate or otherwise influence overall tumor incidence or incidence of particular tumors in either sex of the C57Bl/6J strain, which "generally have been found to have a very low incidence of tumors of any kind" or in the male sex of the "susceptible" C3D2F1/J strain. Likewise, the report concluded that endrin did not affect the incidence of leukemia for females of the C3D2F1/J strain. However, 12 of the 175 endrin-fed C3D2F1/J females developed hepatomas (liver tumors), while only 4 of the 146 C3D2F1/J control females did so. The hepatomas were distributed as follows (listed by age at death or sacrifice):

Kettering Female C3D2F1/J Mouse Study:
Mice with Hepatomas/Mice Examined

Endrin feeding levels, ppm	1-36 weeks	37-44 weeks	45-52 weeks	53-60 weeks	61-68 weeks	69-77 weeks [2]	Total
3.0	0/4	0/12	0/3	5/24	3/14	0/27	8/84 [3]
0.3	0/2	1/15	0/1	0/20	1/22	2/31	4/91
0.0(A)	0/4	0/13	0/0	0/21	0/10	3/36	3/84
0.0(B)	0/3	1/9	0/0	0/23	0/8	0/19	1/62

The report went into a special discussion of the hepatomas in the C3D2F1/J females which had been fed endrin. First, it pointed out that hepatomas occurred in both the 0.3 ppm group and control group B before they occurred in the 3.0 ppm group. Second, it pointed out that hepatomas were not found in mice from the 3.0 ppm group, which were sacrificed last although hepatomas were found in members of control group A which were sacrificed during the same period. Thus the report said the incidence of hepatomas did not consistently increase as a function of dose, nor did the hepatomas occur first in the more heavily-dosed group. The report said that these "discrepancies" in the "assumption" of a time-dose-hepatoma relationship, plus the lack of "convincing" evidence of a dose-response relationship,

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2/ The study was terminated early for females because of a large number of fibroadenomas in all groups.

3/ The report stated that 7 of the 3.0 ppm females had hepatomas, but the appendix to the report shows 8 hepatomas in this group.

led to a conclusion that neither the time of occurrence nor the total incidence of hepatomas in the C3D2F1/J female mice was related to endrin in the diet. The report said that this conclusion was further supported by the lack of endrin-related hepatoma formation in the males of the strain.

Dr. Kuzmack examined the incidence of hepatomas and concluded that the increases in the endrin-fed groups were statistically significant ($p<0.05$) (Appendix BB). Accordingly, Dr. Albert concluded that "there is sufficient indication of oncogenic effect in this study to meet the criteria of 40 CFR 162.11 (a)(3)(ii)(A)" (Appendix AA).

A letter is being prepared to request that Velsicol submit the tissue slides from the Kettering study to EPA for histopathological analysis.

(b) FDA Rat Study

Based on Dr. Reuber's histopathological analysis of the FDA rat study[4/] (Appendix P), the combined incidences of hyperplastic nodules, carcinomas and sarcomas observed in the liver for control and treated groups by Dr. Reuber were:

FDA Rat Study: Rats With Hyperplastic Nodules, Carcinomas, and Sarcomas in the Liver/Rats Examined

	Feeding Level, ppm					
	0.0	0.1	1.0	5	10	25
Male	0/15	5/16	3/18	1/18	3/20	3/19
	0%	31%	17%	6%	15%	16%
Female	0/23	7/23	4/23	2/20	2/18	1/19
	0%	30%	17%	10%	11%	5%

4/ In 1958, the FDA completed a rat feeding study in which groups of 50 Osborne-Mendel rats, evenly divided by sex, were fed diets containing 25, 10, 5, 1, or 0.1 ppm endrin. The pathological analysis of the slides taken from the study was not completed until 1965 (Appendix O). While the pathology report stated that animals fed the lowest dosage, 0.1 ppm endrin, had the greatest number of rats with malignant tumors, the report did not call endrin a carcinogen. This conclusion apparently was based on the observation that the malignant tumors found in the exposed animals did not occur in any particular location in the body and that the incidence of malignant tumors decreased at the higher dosage levels. The Notice of Rebuttable Presumption solicits comments on the relevance of these observations to determining the carcinogenicity of a compound. The current practice of the National Cancer Institute (NCI) is to compare incidences of total tumors in the experimental animals as well as incidences in specific organs. The recently approved "General Criteria for Assessing the Evidence for Carcinogenicity of Chemical Substances" of the NCI does not require an increase in tumors at higher dosage levels to draw a conclusion of carcinogenicity although it states that such an occurrence provides additional evidence of a positive result. Moreover, the FDA report did not contain any data on the incidence of hyperplastic nodules in either control or exposed animals.

Dr. Thorslund has calculated (Appendix CC), that results from the 0.1 ppm dosage group were significant both for females ($p=0.0229$) and both sexes combined ($p<0.025$).

In addition to effects in the liver, Dr. Reuber observed a variety of tumors, mostly carcinomas and sarcomas, elsewhere. Male controls did not develop any tumors or hepatic lesions of any kind. Endrin-fed males developed reticulum cell sarcomas of the lymph nodes and lungs, as well as some rare malignant tumors and carcinomas of the liver, thyroid, and adrenal cortex. Among female controls, 9 of 23 animals developed tumors, 7 in the mammary gland and 2 adenocarcinomas. The endrin-fed females had much larger numbers of mammary tumors, plus stromal cell sarcomas of the endometrium of the uterus, reticulum cell sarcomas of the lung, Kuppfer cell sarcomas of the liver and carcinomas of the liver, thyroid, and adrenal cortex. The combined incidences of malignant tumors observed in all locations by Dr. Reuber were:

FDA Rat Study: Rats With Malignant Tumors/Rats Examined

	Feeding Level, ppm					
	0.0	0.1	1.0	5	10	25
Male	0/15	13/16	6/18	2/18	5/20	8/19
	0%	81%	33%	11%	25%	42%
Female	9/23	20/23	22/23	16/20	12/18	10/19
	39%	87%	96%	80%	67%	53%

Benign tumors, which occurred particularly in the two lowest feeding levels but not in the controls, are not included in this table; they would make the numbers even higher. For

malignant tumors, the results are statistically significant at $p < 0.001$ at the low dose levels (Appendix NN).

These observations indicate an oncogenic effect, however, the Notice of Rebuttable Presumption solicits comments of the observations of noncarcinogenicity made by the FDA. The fact that additional tumors in the treated animals were not concentrated in specific sites does not change the fact that these animals had more tumors than the controls, in amounts that cannot be accounted for by chance alone. Similarly, a decrease of the incidence of tumors at the higher dose levels is not necessarily inconsistent with a carcinogenic effect.

(c) Other Studies

Certain other tests have involved endrin fed to laboratory animals and subsequent histopathological analyses. A study by Deichmann, et al., in 1970 (Appendix R) was performed with Osborne-Mendel rats fed 2, 6, and 12 ppm and did not report an oncogenic effect. However, the control female animals experienced an extremely high tumor incidence of 68% which was not explained.

A general toxicological study on various animals was conducted by Kettering Laboratory in the early 1950's, and is dated July 11, 1953 (Appendix S). A summary of the results was published in 1955 (Appendix T). The published summary stated, regarding oncogenic effects in Carworth rats fed 1, 5, 25, 50, and 100 ppm endrin for two years, that the incidence of neoplasia among the experimental animals was no greater than among the controls. However,

the published report does not contain data on neoplasms or further discussion of oncogenicity.

Three tests have been conducted on dogs fed endrin, but each of them was run for only two years, which is not considered sufficient time to detect oncogenic responses in dogs, and indeed it is questionable whether the studies were conducted for that purpose. A two-year study by Kettering was completed in May 1955 using 18 dogs fed 1 to 50 ppm endrin. (Appendix U). The 1970 Kettering mouse study (Appendix Q) says that this dog study was negative for tumors. A published summary in October 1955 did not discuss oncogenic response, however (Appendix T). A study by FDA completed in 1959 used 15 dogs fed 1 and 5 ppm endrin (Appendix V); apparently it was not analyzed for histopathological findings or published. EPA recently asked Dr. Reuber to examine the tissue slides from this study. He found lesions suggestive of the early stages of an oncogenic response (Appendix V-1). A Kettering study completed in 1969 used 60 dogs fed 0.1, 0.5, 1, 2, and 4 ppm endrin (Appendix W). No oncogenic effect was discussed or reported and the 1970 Kettering mouse study (Appendix Q) cites this study for effects in blood but not for the study of tumor incidence.

NCI is currently finishing an oncogenic study in rats and mice under its bioassay program.. While the study was scheduled to be completed by January 1976, EPA has been

recently advised that issuance of a preliminary draft for review is ~~scheduled for July 13, 1976~~ imminent.

(2) Fetotoxic and Teratogenic Effects in Test Animals.

40 CFR Section 162.11(a)(3)(ii)(B) provides: "A rebuttable presumption shall arise if a pesticide's ingredient(s) . . . . [p]roduces any other chronic or delayed toxic effect in test animals at any dosage up to a level, as determined by the Administrator, which is substantially higher than that to which humans can reasonably be anticipated to be exposed, taking into account ample margins of safety."

In a 1974 study conducted by Ottolenghi, et al., of the National Institute of Environmental Health Sciences (Appendix DD), endrin was found to produce a statistically significant increase in fetotoxicity and teratogenicity in hamsters fed 5 mg/kg ($p < 0.01$) and in mice fed 2.5 mg/kg ($p < 0.01$).[5/] The effects in hamsters included fused rib, cleft palate, webbed foot, and open eye. The effects observed in mice were less dramatic.

Based upon comments submitted by Dr. Chernoff of the EPA Health Effects Research Laboratory, Research Triangle Park, the Validation Committee concluded that no presumption be issued because of teratogenic effects (Appendix X). Dr. Chernoff indicated that the effects seen in the Ottolenghi

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5/ For both species, the dosage selected was approximately one-half the LD_{50} of the species.

study were not necessarily teratogenic effects, but rather could be considered as fetotoxic effects (Appendix EE). However, such a distinction does not influence the issuance of a presumption. Section 162.11(a)(3)(ii)(B) sets criteria of "other chronic or delayed toxic effect[s]" which would include fetotoxic as well as teratogenic effects as a basis for presumption. Moreover, Dr. Chernoff's review did not indicate that the Ottolenghi study was invalid but rather that an alternative interpretation of the data was tenable (Appendix OO). Dr. Chernoff noted that mean fetal weight from treated animals was significantly lower than that of the controls and suggested that a general fetal growth retardation had resulted in a syndrome of effects at day 14 that would have been typical of all fetuses at an earlier stage of development. In addition the observation of fused rib was restricted essentially to the endrin-treated animals and occurred as a single defect leading the authors to conclude that endrin is teratogenic.

Only one feeding level for each species was tested in the above tests, and it was positive. Therefore the question remains open as to what is the lowest level at which fetotoxic or teratogenic effects can be observed, and as to whether it is substantially higher than that "to which humans can reasonably be anticipated to be exposed." In the absence of a level at which there is no demonstrated effect and the subsequent choice of an "ample margin of safety," it must be presumed that current exposure may be sufficient to produce fetotoxic/teratogenic effects in humans.

(3) Effects on Nontarget Organisms

40 CFR Section 162.11(a)(3)(ii)(C) provides: "A rebuttable presumption shall arise if a pesticide's ingredients . . . . [c]an reasonably be anticipated to result in significant local, regional, or national population reductions in nontarget organisms, or fatality to members of endangered species." Data summarized below indicate that endrin has resulted in fatality in an endangered species and significant reductions in nontarget organism populations, requiring the issuance of rebuttable presumptions against registration or continued registration. The Validation Committee reviewed the data and concluded that a presumption could be issued on these grounds (Appendix FF).

(a) Fatality to Members of an Endangered Species

By the early 1960's, the brown pelican had become extinct in the State of Louisiana. This bird is on the Department of Interior List of Endangered Species. Efforts were undertaken to reestablish the bird in Louisiana by introducing birds from Florida; however, in the spring of 1975 a significant decline in the number of adult pelicans occurred and several were found dead by the Louisiana Wildlife and Fisheries Commission. In an effort to determine the cause of death, an analysis of pesticide body burdens was conducted both by the Department of Interior Patuxent Wildlife Research Center and the LSU Feed and Fertilizer Laboratory. The analysis revealed brain tissue levels of endrin which averaged 0.37 ppm (0.18 - 0.70 ppm) (Appendix J,K). Based upon experimental testing with other avian species, such levels are considered to be in the lethal range for endrin (Appendix GG). While residues of other organochlorines were detected in the dead pelicans, the endrin levels were sufficiently high to have been the sole cause of fatality to the pelicans. Therefore, the fatality to the brown pelicans can be reasonably attributed to endrin.

(b) Significant Population Reductions in Nontarget Organisms

Reports submitted to EPA indicate that the use of endrin as a pesticide has caused numerous fish and wildlife kills

resulting in significant local and regional population reductions of nontarget organisms. Data contained in the EPA Pesticide Episode Reporting System (PERS) (Appendix II) indicate that since 1967 endrin has been involved in fifty-two reported fish and wildlife kills with an estimated loss of over 31 million fish of various species. In addition, endrin has been reported involved in eight episodes involving the poisoning of animals other than wildlife, such as cattle. Thirty-seven of the kills were connected with the agricultural use of endrin from the following causes: pesticide runoff (20 episodes) including most frequently runoff after treatment to cotton fields and applications for mouse control; overspray of water bodies during aerial application (4 episodes); and improper container disposal (2 episodes). PERS data also indicate five wildlife kills including 2 episodes of fatality to migratory waterfowl caused by their feeding on endrin-treated seed or grain. It should also be noted that PERS data is not necessarily complete and therefore probably underestimates the actual effects from endrin use.

Thirty-three of the reported episodes involving fish and wildlife were supported by laboratory analyses showing endrin to be present, either alone or with other pesticides and/or their metabolites in the tissues and environmental media sampled.

The Agency has also received data on the widespread fish, wildlife, and domestic animal kills and contamination of large amounts of milk from cattle exposed to endrin which occurred this spring in Kansas and Oklahoma from agricultural uses of endrin (Appendix HH).

In addition, the Agency has recently received a report (Appendix MM) from the Patuxent Wildlife Research Center regarding thirty-six white pelicans found dead in the Tulelake California area in 1975. Of the eleven brain samples which could be analyzed, Patuxent reported that the endrin levels found in nine of the birds would have been sufficient to cause death. The U.S. Fish and Wildlife Service is currently conducting further investigation into the Tulelake episode.

The available data indicate that the use of endrin can be reasonably anticipated to result in local and regional population reductions of nontarget organisms.

B. Acute Toxicity

40 CFR Section 162.11(a)(3)(i) sets forth several criteria which require that a rebuttable presumption arise because of the acute toxicity of the pesticide to humans and domestic animals (§162.11(a)(3)(i)(A)), and to wildlife (§162.11(a)(3)(i)(B)). As discussed in the preamble to 40 CFR Part 162 (40 FR 28262), pesticides which meet or exceed the acute toxicity criteria of Section 162.11(a)(3)(i) must be closely

scrutinized to determine if the hazard indicated by the acute toxic[illegible]acteristics of the pesticides necessitate restrictions on use, or denial or cancellation of the registrations.

Data indicate that pesticide products formulated with endrin may meet or exceed the acute toxicity criteria set forth in Section 162.11(a)(3)(i)(A) and (B), depending upon the endrin concentration in a product and other characteristics of a product's specific formulation. Therefore, to determine if a specific product meets or exceeds the acute toxicity criteria of Section 162.11(a)(1)(A) and (B), the toxicity of each individual product and each of its uses dilutions must be determined. ~~by testing or extrapolation.~~ Accordingly, based upon the acute toxicity studies of endrin set forth below or such other studies as the registrant may submit to the Agency, each registrant is directed in the Notice of Rebuttable Presumption to determine the acute toxicity of each formulation as well as each dilution registered for use and determine whether or not the criteria of Section 162.11(a)(3)(i)(A) and (B) are met or exceeded. If the criteria are met or exceeded, a rebuttable presumption shall arise and the registrant is directed to submit rebuttal evidence pursuant to Section 162.11(a)(4). The procedure of registrant certification of acute toxicity determinations is being utilized for

endrin to estimate the feasibility of the procedure for other rebuttable presumption determinations.

(1) Hazards to Humans and Domestic Animals

Data indicate that endrin when formulated as a 19.2% weight/volume (w/v) emulsifiable concentrate has an acute dermal median lethal dose (LD_{50}) of 11.3 mg/kg, that a 20% formulation has an acute dermal LD_{50} of 10.9, and that a 2% dust has an acute dermal LD_{50} of 31.5 mg/kg for rats (Appendix KK). Section 162.11(a)(3)(i)(A)(1) provides that a rebuttable presumption shall be issued if the pesticide as formulated has an acute dermal LD_{50} of 40 mg/kg or less. Accordingly, the notice directs each registrant to certify to the Agency whether or not: (1) the pesticide as formulated has an acute dermal LD_{50} of 40 mg/kg or less; (2) the pesticide has an acute dermal LD_{50} of 6g/kg or less as diluted for use in the form of a mist or spray; or (3) the pesticide has an inhalation LC_{50} of 0.04 mg/liter or less as formulated. The certification shall specify the acute dermal LD_{50} of the formulation and the calculations and data relied upon in making that determination.

(2) Hazard to Wildlife

Section 162.11(a)(3)(i)(B)(1) and (2) provides that a rebuttable presumption shall be issued if the pesticide as formulated occurs as a residue immediately following application in or on the feed of a mammalian or avian species

representative of species likely to be exposed to such feed in amounts equivalent to the average daily intake at levels equal to or greater than (1) the acute oral LD_{50} for mammalian species and (2) the subacute dietary LC_{50} for avian species.

Since registrations of endrin products may result in mammalian and avian feed residues, calculations have been completed to determine if the criteria of Section 162.11(a)(3)(i)(B)(1) and (2) are met or exceeded. Those calculations (Appendix LL) indicate that a 1.2 or greater lb/acre formulation of endrin sprayed on grasses and forbs of apple orchards for the control of mice will result in feed residues on grasses of 290 ppm and forage of 145 ppm which meet or exceed the acute oral LD_{50} of rabbits (7 mg/kg) based upon the estimated average daily intake of such feed. Such use of endrin on orchards also will result in estimated residues on seeds of 14 ppm, which equal the subacute dietary LC_{50} for quail and pheasant (14 ppm). In addition, application to small grain crops at 3.2 oz or greater/acre will result in estimated residues which meet or exceed the acute oral LC_{50} for rabbits. Accordingly, the presumption notice directs each registrant of an endrin product for controlling orchard mice to certify to the Agency whether or not the formulation is for 1.2 or greater lb/acre or whether or not small grain registrations are 3.2 oz or greater/acre and to certify whether the

registered use will result in residues on the feed of wildlife from direct application and, if so, whether or not the residues, either estimated or measured, meet or exceed the criteria for acute hazard to wildlife. If the registrant certifies that the product meets these criteria and therefore that a presumption exists, the registrant is directed to submit rebuttal evidence pursuant to Section 162.11(a)(4).

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List of Appendices

A. Edwards, C. A. Persistent pesticides in the environment. Selected pages.

B. Barbehenn memo: Loss rate of endrin in fish, 6/24/76.

Moriarty, F. Organochlorine insecticides: Persistent organic pollutants.

C. Bedford, C. T., et al. The acute toxicity of endrin and its metabolites to rats.

D. Endrin Production, 1974-75. CONFIDENTIAL.

E. Axelrod memo: Position paper on endrin, 11/8/73.

Hartwell/Dale memo: Suggested actions on the pesticidal use of endrin, 11/6/73.

F. Environmental Defense Fund: Petition for the Suspension and Cancellation of the Pesticide Endrin, 7/31/75.

G. Velsicol Chemical Corporation: Response to Petition for the Suspension and Cancellation of the Pesticide Endrin, 11/10/75.

H. Environmental Defense Fund renewal petition: Suspension and/or Cancellation of the Pesticide Endrin, 4/30/76.

I. Audubon report: Pesticides Deciminate Transplanted Pelicans, 9/75.

J. Barbehenn memos: Brown Pelican Mortality in Louisiana, 6/24/76.

Laboratory reports on brown pelican samples submitted by Dr. John Newson, Louisiana State University.

Murphy memo of 1/29/76 forwarding report on brown pelican kill in Louisiana.

K. Stickel letter of 2/23/76 forwarding autopsy reports on brown pelicans killed in Louisiana.

L. Unpublished Fish and Wildlife Service reports on primary and secondary wildlife poisonings from endrin-treated pine seeds.

M. Barbehenn memo: Control of orchard mice, 6/24/76.

N. List of EPA-registered pesticide products containing endrin as an active ingredient, 12/22/75.

O. FDA Pathological Study of Rats Fed Endrin or Dieldrin for Two Years, 9/2/65.

P. Reuber analysis of the tissue slides from the FDA endrin rat study, 6/1/76.

Q. Kettering Laboratory. The Incidence of Neoplasms in Two Strains of Mice Sustained on Diets Containing Endrin. 6/17/70. CONFIDENTIAL.

R. Deichmann, W. B. et al. Tumorigenicity of aldrin, dieldrin, and endrin in the albino rat.

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